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EXAMINER	
KATCHEVES, KONSTANTINA T	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,267	KUNDRA, VIKAS	
	Examiner	Art Unit	
	Konstantina Katcheves	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 26-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-25* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/14/02; 7/5/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-36 are pending in the present application. Claims 1-9 and 26-36 have been withdrawn from consideration. Claims 10-25 are currently under examination.

Election/Restrictions

Applicant's election without traverse of Group II, claims 16-25, in the reply filed on 26 March 2004 is acknowledged. Claims 1-15 and 26-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 26 March 2004.

Claim Objections

Claim 10 is objected to because of the following informalities: Claim 10 depends from non-elected claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The instant claims are drawn to fusion proteins. This is a very broad genus which on a broad genus of proteins. Such a generic recitation of fusion protein comprises practically any fusion of proteins, their mutants, variants, or fragment. Neither the claims nor the specification, as filed, indicate what distinguishing attributes the members of this very broad genus of proteins share. Thus, the scope of the claims includes numerous members, which permits significant number of structural differences between the genus members. The specification and claims both fail to provide guidance as to what the defining characteristics of these fusion proteins are either in terms of structure or function.

The specification only discloses that the fusion protein comprises a reporter that may be a somatostatin receptor (SSTR) or a SSTR that has been mutated by deleting

all or part of its intracellular domain. The claims however are very broad which include many other components of the fusion protein. Additionally, the single disclosure of SSTR or mutant SSTR is not sufficient to define all fusion proteins embraced by the genus. Moreover, claims 18 and 19 are limited to ligands which bind to mutated somatostatin receptors and mutated somatostatin type 2 receptor, the specification still fails to disclose a structure-function relationship between somatotostatin receptors and mutated somatostatin type 2 receptors for the foregoing reasons.

Since the disclosure fails to describe common attributes or characteristics that identify the members of the genus and since the genus is very broad, the disclosure alone is not sufficient to describe the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claims 16-25 are drawn to transferring a "gene" into a host cell. The word "gene" refers not only to a coding sequence but also to an entire genomic structure. Genomic structure includes introns and all regulatory regions upstream and downstream of coding sequences. The word "gene" represents a broad genus of molecules for which the entire genomic structure of a representative number of eukaryotic "genes" is not known. Therefore, these claims fail to describe the broad genus of genes with such descriptive means to adequately describe the present invention. One of skill in the art could not reasonably conclude that Applicant is in possession of the broad genus of genes claim. It is suggested that the word gene be replaced with terminology such as "nucleic acid sequence".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-25 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is drawn to "an expression vector according to claim 10." Claim 10 does not claim an expression vector, while claim 11 does. Therefore, the present claim is unclear.

Claims 18 and 19 recite the following limitations:

> Claim 18. . . .contacting said host cell with a ligand that binds with speciticity to a somatostatin receptor, or mutated somatostatin receptor, and wherein said ligand has been detectably labeled.
> Claim 19. . . .contacting said host cell with a ligand that binds with specificity to a somatostatin type 2 receptor, or mutated somatostatin type 2 receptor, and wherein said ligand has been detectably labeled.

These claims are inherently unclear because a number of plausible interpretations of these claims are possible. Do these claim refer to a receptor that is a moiety of the fusion protein encoded by the nucleic acid of claim 10? Is the "ligand" recited in these claims a moiety of the fusion protein, or is the fusion protein identified by an intermediate interaction between a ligand and receptor, neither of which being a moiety of the fusion protein? Multiple interpretations of these claims are possible because there is no nexus between the limitations of these method claims and the polynucleotide of claim 10.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10-17 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Glucksmann et al. (US 2003/0166061 A1).

The invention of the instant claims is drawn to a nucleic acid encoding a fusion protein comprising a reporter, polypeptide and leader sequence which are defined on page 4 of the specification as signal sequences. The present claims are drawn to vector constructs and host cells comprising the nucleic acid. Claims 16, 17 and 24 are drawn to methods of assaying for the expression of the fusion protein described above comprising transferring the vector into a host cells and assaying expression based on the chemical, physical or biological properties of the fusion protein.

Glucksmann et al. disclose constructs encoding and host cells comprising a GST-receptor fusion proteins attached to a signal sequence. See page 8, paragraph [0097] and page 21, paragraph [0253], [0254], [0264] to [0271]. Glucksmann et al. wherein expression of a fusion protein is identified in a transgenic animal based on the expression of mRNA in tissues or cells of the animals. See page 24, paragraph [0299].

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-18, 20, 21 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glucksmann et al. as applied to claims 10-17 and 24 above, and further in view of Eisenhut et al. (US 2001/0029035).

The invention of the instant claims is drawn to methods of assaying for the expression of the fusion protein described above comprising transferring the vector into a host cells and assaying expression based on the chemical, physical or biological properties of the fusion protein. The expression of the fusion protein is measured by contacting the host cell with a ligand, wherein said ligand is a radioactively labeled octreotide. Although the product does not specifically claim a somatostatin receptor as part of the claimed fusion protein, based on the recitation of the method it is presumed that the fusion protein comprises a somatostatin receptor.

Glucksmann et al. disclose constructs encoding and host cells comprising a GST-receptor fusion proteins attached to a signal sequence. See page 8, paragraph [0097] and page 21, paragraph [0253], [0254],[0264] to [0271]. Glucksmann et al. wherein expression of a fusion protein is identified in a transgenic animal based on the expression of mRNA in tissues or cells of the animals. See page 24, paragraph [0299].

Eisenhutt et al. teach the use of a PNA peptide conjugate, which includes octreotide, labeled with ^{125}I to determine distribution of the conjugate in organs. See

page 6, example 7, paragraph [0057] and [0069]-[0072]. Eisenhutt et al. teach that octreotides are somatostatin analogs which bind the somatostatin receptor. See page 2, paragraph [0012], [0015] and [0016].

It would have been obvious to one of ordinary skill in the art to use radioactive octreotides to measure expression of fusion proteins that comprise somatostatin receptors. One of ordinary skill in the art would have been motivated to use radioactively labeled somatostatin analogs because they would allow for one of skill in the art to identify expressed fusion proteins comprising somatostatin receptors because, as taught by Eisenhutt et al., these analogs would bind the receptor portion of the fusion protein. One of ordinary skill in the art would reasonably expect the binding of a radioactive somatostatin analog to the receptor portion of a fusion protein to successfully confirm the expression of the fusion protein because binding assays are within the purview of the ordinary skilled artisan. Moreover, such a binding assay was taught by Eisenhutt et al. to identify distribution of octreotide analogs. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 10-16 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glucksmann et al. as applied to claims 10-17 and 24 above, and further in view of Koller et al. (Analytical Biochemistry Vol.250 pp51-60 1997).

The invention of the instant claims is drawn to methods of assaying for the expression of the fusion protein described above comprising transferring the vector into a host cells and assaying expression based on the chemical, physical or biological

properties of the fusion protein. The expression of the fusion protein is measured by contacting the host cell with a an antibody which binds the fusion protein and more specifically binds hemagglutinin A. Although the product does not specifically claim hemagglutinin A as part of the claimed fusion protein, based on the recitation of the method it is presumed that hemagglutinin A is part of the fusion protein.

Glucksmann et al. disclose constructs encoding and host cells comprising a GST-receptor fusion proteins attached to a signal sequence. See page 8, paragraph [0097] and page 21, paragraph [0253], [0254], [0264] to [0271]. Glucksmann et al. wherein expression of a fusion protein is identified in a transgenic animal based on the expression of mRNA in tissues or cells of the animals. See page 24, paragraph [0299].

Koller et al. teach the use of a hemagluttanin A sequence fused to a receptor as a means of identifying the expressed receptors. The expressed protein is identified by the binding of hemagglutinin A to the commercially available antibody, 12CA5. See page 51, column 2 and page 52 column 1, paragraph 1 and 2.

It would have been obvious to one of ordinary skill in the art to use antibodies that bind the antibodies that bind hemagglutinin A to measure expression of the fusion proteins of the invention that comprise hemagglutinin A. One of ordinary skill in the art would have been motivated to use antibodies because they allow for one of skill in the art to identify expressed fusion proteins that comprise particular sequences and structural characteristics to which the antibodies bind. Koller et al. teach hemagluttin A and the antibody, 12CA5, to identify hemagglutinin A/receptor fusion proteins. One of ordinary skill in the art would reasonably expect the binding of an antibody to its respective ligand to be able to identify the expression of a target protein. As exemplified by Koller et al.,

binding assays are well known in the art and well within the purview of the ordinary skilled artisan. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 10-16 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glucksmann et al. as applied to claims 10-16 and 24 above, and further in view of Ausubel et al. (Short Protocols in Molecular Biology 1999).

The invention of the instant claims is drawn to methods of assaying for the expression of the fusion protein described above comprising transferring the vector into a host cells and assaying expression based on the chemical, physical or biological properties of the fusion protein. The expression of the fusion protein is measured by contacting the host cell with a an antibody which binds the fusion protein and more specifically binds hemagglutinin A. Although the product does not specifically claim hemagglutinin A as part of the claimed fusion protein, based on the recitation of the method it is presumed that hemagglutinin A is part of the fusion protein.

Glucksmann et al. disclose constructs encoding and host cells comprising a enzyme-receptor fusion proteins attached to a signal sequence. See page 8, paragraph [0097] and page 21, paragraph [0264] to [0271]. Glucksmann et al. wherein expression of a fusion protein is identified in a host based on the expression of mRNA in cells. See page 24, paragraph [0253], [0254], [0299]. Glucksmann et al. fail to teach enzymatic fusion comprising chloramphenicol acetyltransferase (CAT).

Ausubel et al. (Short Protocols in Molecular Biology 4th Ed. 1999) teach common enzymatic reporters including CAT. See page 9-27 and page 9-31.

It would have been obvious to one of ordinary skill in the art to use enzyme fusion proteins in order to identify expression of the fusion protein construct based on detection of the enzymatic activity. One of ordinary skill in the art would have been motivated to use CAT because it is one of may common reporter genes known in the art. Moreover, it is useful because minimal endogenous activity of CAT is found in mammalian cells so that those of ordinary skill in the art would be assured that they are measuring expression of the fusion protein and not background expression of CAT. One of ordinary skill in the art would reasonably expect the successful use of enzyme fusion proteins using CAT as the enzyme because the use of reporters is germane to the art of molecular biology. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (571) 272-0768. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday 7:30 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Konstantina Katcheves
Examiner
Art Unit 1636